

# Amendments to the Claims

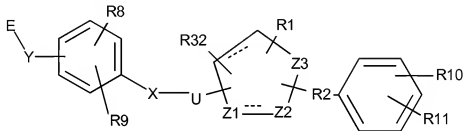
Please cancel claims: 4, 7, 40, 55, 60, 61, 62, 66, and 67

## In the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

What is claimed is:

1. (Currently amended) A compound of the Formula I':



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

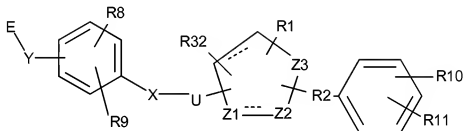
- (a) R1 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, and, wherein C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>0-4</sub>-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)<sub>2</sub>R16, N(R17)<sub>2</sub>, NR18C(O)R19, NR20SO<sub>2</sub>R21, SR22, S(O)R23, S(O)<sub>2</sub>R24, and S(O)<sub>2</sub>N(R25)<sub>2</sub>; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (c) R2 is selected from the group consisting of C<sub>0</sub>-C<sub>8</sub> alkyl and C<sub>1-4</sub> heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)<sub>2</sub> and N;

- (e) U is an aliphatic linker ~~wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S,~~ and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;
- (f) Y is selected from the group consisting of C, NH, and a single bond;
- (g) E is C(R3)(R4)A and wherein
  - (i) A is selected from the group consisting of carboxyl, tetrazole, C<sub>1</sub>-C<sub>6</sub> alkyl nitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R<sup>7</sup>;
  - (ii) each R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl C<sub>0</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl;
  - (iii) R3 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy; and
  - (iv) R4 is selected from the group consisting of H, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R3 and R4 are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with from one to three substituents each independently selected from R26;
- (h) Z1 and Z2 are each ~~independently selected from the group consisting of N, O, and C with the proviso that at least one of Z1 and Z2 is N;~~
- (i) Z3 is ~~selected from the group consisting of N, O, and C;~~
- (j) R8 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, and halo;
- (k) R9 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, halo, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl, C<sub>1</sub>-C<sub>6</sub> allyl, and OR29, and wherein aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;
- (l) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12'', C<sub>0</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, aryloxy,

$C(O)R13'$ ,  $COOR14'$ ,  $OC(O)R15'$ ,  $OS(O)_2R16'$ ,  $N(R17')_2$ ,  $NR18'C(O)R19'$ ,  $NR20'SO_2R21'$ ,  $SR22'$ ,  $S(O)R23'$ ,  $S(O)_2R24'$ , and  $S(O)_2N(R25')_2$ ; and wherein aryl- $C_{0-4}$ -alkyl, aryl- $C_{1-4}$ -heteroalkyl, heteroaryl- $C_{0-4}$ -alkyl, and C3-C6 cycloalkylaryl- $C_{0-2}$ -alkyl are each optionally substituted with from one to three independently selected from R28;

- (m)  $R12'$ ,  $R12''$ ,  $R13'$ ,  $R14'$ ,  $R15'$ ,  $R16'$ ,  $R17'$ ,  $R18'$ ,  $R19'$ ,  $R20'$ ,  $R21'$ ,  $R22'$ ,  $R23'$ ,  $R24'$ , and  $R25'$  are each independently selected from the group consisting of hydrogen,  $C_1$ - $C_6$  alkyl and aryl;
- (n) R30 is selected from the group consisting of  $C_1$ - $C_6$  alkyl, aryl- $C_{0-4}$ -alkyl, aryl- $C_{1-4}$ -heteroalkyl, heteroaryl- $C_{0-4}$ -alkyl, and C3-C6 cycloalkylaryl- $C_{0-2}$ -alkyl, and wherein  $C_1$ - $C_6$  alkyl, aryl- $C_{0-4}$ -alkyl, aryl- $C_{1-4}$ -heteroalkyl, heteroaryl- $C_{0-4}$ -alkyl, and C3-C6 cycloalkylaryl- $C_{0-2}$ -alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
- (o) R32 is selected from the group consisting of a bond, hydrogen, halo,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  haloalkyl, and  $C_1$ - $C_6$  alkoxy; and
- (p) --- is optionally a bond to form a double bond at the indicated position.

2. (Currently amended) A compound of the Formula I'':

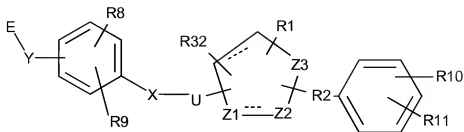


and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkenyl, aryl- $C_{0-4}$ -alkyl, aryl- $C_{1-4}$ -heteroalkyl, heteroaryl- $C_{0-4}$ -alkyl, and C3-C6 cycloalkylaryl- $C_{0-2}$ -alkyl, and, wherein  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkenyl, aryl- $C_{0-4}$ -alkyl, aryl- $C_{1-4}$ -heteroalkyl, heteroaryl- $C_{0-4}$ -alkyl, C3-C6 cycloalkylaryl- $C_{0-2}$ -alkyl are each optionally substituted with from one to three substituents independently selected from R1';

- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sub>12</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>0</sub>-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R<sub>13</sub>, COOR<sub>14</sub>, OC(O)R<sub>15</sub>, OS(O)<sub>2</sub>R<sub>16</sub>, N(R<sub>17</sub>)<sub>2</sub>, NR<sub>18</sub>C(O)R<sub>19</sub>, NR<sub>20</sub>SO<sub>2</sub>R<sub>21</sub>, SR<sub>22</sub>, S(O)R<sub>23</sub>, S(O)<sub>2</sub>R<sub>24</sub>, and S(O)<sub>2</sub>N(R<sub>25</sub>)<sub>2</sub>; R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, R<sub>24</sub> and R<sub>25</sub> are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (c) R2 is selected from the group consisting of C<sub>0</sub>-C<sub>8</sub> alkyl and C<sub>1</sub>-4 heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)<sub>2</sub> and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is substituted with from one to four substituents each independently selected from R<sub>30</sub>;
- (f) Y is selected from the group consisting of C, and S;
- (g) E is C(R<sub>3</sub>)(R<sub>4</sub>)A or A and wherein
  - (i) A is selected from the group consisting of carboxyl, tetrazole, C<sub>1</sub>-C<sub>6</sub> alkyl nitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R<sup>7</sup>;
  - (ii) each R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl C<sub>0</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl;
  - (iii) R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy; and
  - (iv) R<sub>4</sub> is selected from the group consisting of H, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R<sub>3</sub> and R<sub>4</sub> are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with from one to three substituents each independently selected from R<sub>26</sub>;
- (h) Z1 and Z2 are each independently selected from the group consisting of N, O, and C with the proviso that at least one of Z1 and Z2 is N;
- (i) Z3 is selected from the group consisting of N, O, and C;

- (j) R8 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, and halo;
  - (k) R9 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, halo, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl, C<sub>1</sub>-C<sub>6</sub> allyl, and OR29, and wherein aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;
  - (l) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12'', C<sub>0</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)<sub>2</sub>R16', N(R17')<sub>2</sub>, NR18'C(O)R19', NR20'SO<sub>2</sub>R21', SR22', S(O)R23', S(O)<sub>2</sub>R24', and S(O)<sub>2</sub>N(R25')<sub>2</sub>; and wherein aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl are each optionally substituted with from one to three independently selected from R28;
  - (m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
  - (n) R30 is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, and wherein C<sub>1</sub>-C<sub>6</sub> alkyl, aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
  - (o) R32 is selected from the group consisting of a bond, hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, and C<sub>1</sub>-C<sub>6</sub> alkyloxy; and
  - (p) ---- is optionally a bond to form a double bond at the indicated position.
3. (currently amended) A compound as claimed by Claim 2 of the Formula I''':



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C3-C6 cycloalkylaryl-C<sub>0-2</sub>-alkyl, and, wherein C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C3-C6 cycloalkylaryl-C<sub>0-2</sub>-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>0-4</sub>-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)<sub>2</sub>R16, N(R17)<sub>2</sub>, NR18C(O)R19, NR20SO<sub>2</sub>R21, SR22, S(O)R23, S(O)<sub>2</sub>R24, and S(O)<sub>2</sub>N(R25)<sub>2</sub>; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (c) R2 is selected from the group consisting of C<sub>0</sub>-C<sub>8</sub> alkyl and C<sub>1-4</sub> heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)<sub>2</sub> and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;
- (f) Y is selected from the group consisting of S and C;
- (g) E is C(R3)(R4)A; wherein
  - (i) A is selected from the group consisting of carboxyl, tetrazole, C<sub>1</sub>-C<sub>6</sub> alkyl nitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide,

acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R<sup>7</sup>;

(ii) each R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl C<sub>0</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl;

(iii) R<sub>3</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy; and

(iv) R<sub>4</sub> is selected from the group consisting of H, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R<sub>3</sub> and R<sub>4</sub> are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with from one to three substituents each independently selected from R<sub>26</sub>;

with the proviso that when Y is O then R<sub>4</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R<sub>3</sub> and R<sub>4</sub> are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three each independently selected from R<sub>26</sub>;

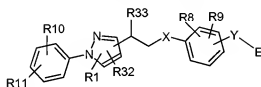
- (h) Z<sub>1</sub> and Z<sub>2</sub> are each ~~independently selected from the group consisting of N, O, and C~~ with the proviso that at least one of Z<sub>1</sub> and Z<sub>2</sub> is N;
- (i) Z<sub>3</sub> is ~~selected from the group consisting of N, O, and C~~;
- (j) R<sub>8</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, and halo;
- (k) R<sub>9</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, halo, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl, C<sub>1</sub>-C<sub>6</sub> allyl, and OR<sub>29</sub>, and wherein aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R<sub>27</sub>; R<sub>29</sub> is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;
- (l) R<sub>10</sub>, R<sub>11</sub> are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sub>12</sub>'', C<sub>0</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, aryl-C<sub>1</sub>-C<sub>4</sub>-heteroalkyl, heteroaryl-C<sub>0</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-C<sub>2</sub> alkyl, aryloxy, C(O)R<sub>13</sub>', COOR<sub>14</sub>', OC(O)R<sub>15</sub>', OS(O)<sub>2</sub>R<sub>16</sub>', N(R<sub>17</sub>')<sub>2</sub>, NR<sub>18</sub>'C(O)R<sub>19</sub>', NR<sub>20</sub>'SO<sub>2</sub>R<sub>21</sub>', SR<sub>22</sub>', S(O)R<sub>23</sub>', S(O)<sub>2</sub>R<sub>24</sub>', and S(O)<sub>2</sub>N(R<sub>25</sub>')<sub>2</sub>; and wherein aryl-

- C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C3-C6 cycloalkylaryl-C<sub>0-2</sub>-alkyl are each optionally substituted with from one to three independently selected from R28;
- (m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (n) R30 is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C3-C6 cycloalkylaryl-C<sub>0-2</sub>-alkyl, and wherein C<sub>1</sub>-C<sub>6</sub> alkyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C3-C6 cycloalkylaryl-C<sub>0-2</sub>-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
- (o) R32 is selected from the group consisting of a bond, hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, and C<sub>1</sub>-C<sub>6</sub> alkoxy; and
- (p) ---- is optionally a bond to form a double bond at the indicated position.
4. (Canceled)
5. (Withdrawn) A compound as claimed by any one of Claims 1 or 2 wherein X is -O-.
6. (Withdrawn) A compound as claimed by any one of Claims 1 or 2 wherein X is -S-.
7. (Canceled)
8. (Previously amended) A compound as claimed by Claim 2 wherein Y is C.
9. ((Previously amended) A compound as claimed by Claim 2 wherein Y is S.
10. (Withdrawn) A compound as claimed by any one of Claims 1 or 2 wherein Z3 is N.
11. (Withdrawn) A compound as claimed by any one of Claims 1 or 2 wherein Z3 is O.
12. (Withdrawn) A compound as claimed by any one of Claims 1 or 2 wherein Z2 is N.
13. (Withdrawn) A compound as claimed by any one of Claims 1, or 2 wherein Z1 is C.
14. (Withdrawn) A compound as claimed by any one of Claims 1 or 2 wherein Z1 is N.
15. (Withdrawn) A compound as claimed by any one of Claims 1 or 2 wherein Z1 is O.
16. (Previously amended) A compound as claimed by any one of Claims 1 or 2 wherein ---- is a bond to form a double bond at the designated location on Formula I.
17. (Previously amended) A compound as claimed by Claim 14 wherein E is C(R3)(R4)A.
18. (Previously amended) A compound as claimed by any one of Claims 1 or 2 wherein A is COOH.



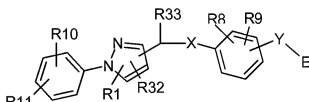
19. (Previously amended) A compound as claimed by Claim 18 wherein R10 is haloalkyl.
20. (Previously amended) A compound as claimed by Claim 18 wherein R10 is CF<sub>3</sub>.
21. (Previously amended) A compound as claimed by Claim 18 wherein R10 is haloalkyloxy.
22. (Previously amended) A compound as claimed by Claim 18 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sup>12''</sup>, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, and C<sub>1</sub>-C<sub>6</sub> haloalkyloxy.
23. (Previously amended) A compound as claimed by Claim 18 wherein R10 is selected from the group consisting of C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, and aryloxy.
24. (Previously amended) A compound as claimed by Claim 2 wherein R1 is optionally substituted C2-C3 arylalkyl.
25. (Previously amended) A compound as claimed by Claim 18, wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>3</sub> alkyl.
26. (Previously amended) A compound as claimed by Claim 18 wherein R1, R2, R3, and R4 are each independently selected from the group consisting of C<sub>1</sub>-C<sub>2</sub> alkyl.
27. (Previously amended) A compound as claimed by Claim 18 wherein R1, R3, and R4 are each independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>2</sub> alkyl.
28. (Previously amended) A compound as claimed by Claim 18 wherein R2 is a bond.
29. (Previously amended) A compound as claimed by Claim 18 wherein U is C<sub>1</sub>-C<sub>3</sub> alkyl.
30. (Previously amended) A compound as claimed by Claim 1 wherein U is saturated.
31. (Previously amended) A compound as claimed by Claim 18 wherein U is substituted with C<sub>1</sub>-C<sub>3</sub> alkyl.
32. (Withdrawn) A compound as claimed by Claim 29 wherein one carbon of the aliphatic linker is replaced with an O.
33. (Withdrawn) A compound as claimed by Claim 18 wherein U is an aliphatic linker having one carbon replaced by S.
34. (Previously amended) A compound as claimed by Claim 18 wherein the aliphatic linker is substituted with from one to three substituents each independently selected from R30.
35. (Original) A compound as claimed by Claim 34 wherein the aliphatic linker is substituted with from one to two substituents each independently selected from R30.

36. (Previously amended) A compound as claimed by Claim 18 wherein each R30 is independently selected from the group consisting of C1-C6 alkyl.
37. (Previously amended) A compound as claimed by Claim 36 wherein each R30 is independently selected from the group consisting of C2-C3 alkyl.
38. (Previously amended) A compound as claimed by Claim 34 wherein R30 is selected from the group consisting of aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C3-C6 cycloalkylaryl-C<sub>0-2</sub>-alkyl.
39. (Withdrawn) A compound as claimed by Claim 18 wherein “---” each form a double bond in the five membered ring, Z2 and Z3 are each N and Z3 is bonded to R2.
40. (Canceled)
41. (Previously amended) A compound as claimed by Claim 36 wherein U is substituted with methyl.
42. (Previously amended) A compound as claimed by Claim 29 wherein U is methylene.
43. (Previously amended) A compound as claimed by any one of Claims 1 or 2 or represented by the following Structural Formula II:



wherein R33 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>3</sub> alkyl.

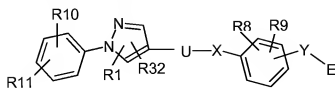
44. (Previously amended) A compound as claimed by Claim 18 represented by the



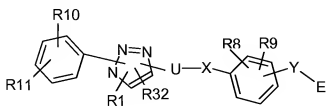
following Structural Formula III:

wherein R33 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>3</sub> alkyl.

45. (Previously amended) A compound as claimed by Claim 18 represented by the following Structural Formula IV:



46. (Withdrawn) A compound as claimed by Claim 18 represented by the following  
Structural Formula V:



47. (Previously amended) A compound as claimed by Claim 18 wherein X and Y are substituted at a 1,4-position, such that X and Y are para substituted to one another.  
48. (Previously amended) A compound as claimed by Claim 18 wherein X and Y are substituted at a 1,3-position, such that X and Y are meta substituted to one another.  
49. (Withdrawn) A compound as claimed by Claim 18 wherein the compound is selected

from the group consisting of

(3-{1-[3-Methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenyl)-acetic acid;

(3-{1-[3-Methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethoxy}-phenyl)-acetic acid;

(4-{1-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-2-methyl-phenoxy)-acetic acid;

3-(4-{1-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-2-methyl-phenyl)-propionic acid;

3-{4-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethylsulfanyl]-2-methyl-phenyl}-propionic acid;

{4-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethylsulfanyl]-2-methyl-phenoxy}-acetic acid;

{4-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethylsulfanyl]-2-methyl-phenoxy}-acetic acid;

3-{4-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethylsulfanyl]-2-methyl-phenyl}-propionic acid;

{3-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-phenyl}-acetic acid;

3-{4-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-2-methyl-phenyl}-propionic acid;

(S)-3-{4-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-phenyl}-2-methoxy-propionic acid;

{3-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-phenyl}-acetic acid;

3-{4-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-2-methyl-phenyl}-propionic acid;

3-{4-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-phenyl}-2-methoxy-propionic acid;

3-[2-Methyl-4-(3-methyl-1-phenyl-1H-pyrazol-4-ylmethoxy)-phenyl]-propionic acid;  
{2-Methyl-4-[5-methyl-1-(4-trifluoromethyl-phenyl)-1H-[1,2,3]triazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

3-{2-Methyl-4-[4-methyl-3-(4-trifluoromethyl-phenyl)-isoxazol-5-ylmethoxy]-phenyl}-propionic acid;

{4-[5-Isopropyl-2-(4-trifluoromethyl-phenyl)-3H-imidazol-4-ylmethylsulfanyl]-2-methyl-phenoxy}-acetic acid; {4-[5-Isopropyl-3-methyl-2-(4-trifluoromethyl-phenyl)-3H-imidazol-4-ylmethylsulfanyl]-2-methyl-phenoxy}-acetic acid;

{4-[5-Isopropyl-3-methyl-2-(4-trifluoromethyl-phenyl)-3H-imidazol-4-ylmethoxy]-2-methyl-phenoxy}-acetic acid; and

3-{4-[5-Isopropyl-3-methyl-2-(4-trifluoromethyl-phenyl)-3H-imidazol-4-ylmethoxy]-2-methyl-phenyl}-propionic acid.

50. (Withdrawn) A compound as claimed by Claim 18 which is a compound of Formula I selected from the group consisting of (R)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid, (S)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid, (R,S)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-propylsulfanyl}-phenoxy)-acetic acid, and (R,S)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid.

51. (Withdrawn) A compound as claimed by Claims 1 which is (R,S)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid.
52. (Previously amended) A compound as claimed by Claim 2 that is the S conformation.
53. (Previously amended) A compound as claimed by Claim 2 that is the R conformation.
54. (Previously amended) A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by Claim 18, together with a pharmaceutically acceptable carrier or diluent.
55. (Canceled)
56. (Previously amended) A method of treating diabetes mellitus in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claim 18.
57. (Previously amended) A method of treating metabolic disorder in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claim 18.
58. (Original) A method of Claim 57 wherein the mammal in need thereof is diagnosed as suffering from metabolic disorder.
59. (Previously amended) A method of selectively modulating a PPAR delta receptor comprising administering a compound as claimed by Claim 2 to a mammal in need thereof.
60. (Canceled)
61. (Canceled)
62. (Canceled)
63. (Previously amended) A method for treating or preventing the progression of cardiovascular disease in a mammal in need thereof comprising administering a therapeutically effective amount of a compound as Claimed by Claim 18.
64. (Original) A method as claimed by Claim 63 wherein the mammal is diagnosed as being in need of such treatment.
65. (Previously amended) A compound as claimed by Claim 18 wherein the compound is radiolabeled.
66. (Canceled)
67. (Canceled)